

IN THE CLAIMS:

Cancel claims 2, 6, 10, 12 and 18.

1. (Currently Amended) An isolated nucleic acid molecule of an alternative splicing variant of a human voltage-gated calcium channel subunit, comprising a sequence of nucleotides encoding a voltage-gated calcium channel $\alpha_2\delta_2$ -a subunit selected from the group consisting of:

- (a) a sequence of nucleotides that encodes a human voltage-gated calcium channel $\alpha_2\delta_2$ -a subunit residues and comprises the sequence of nucleotides set forth in SEQ IDNo:1;
- (b) a sequence of nucleotides that encodes a human voltage-gated calcium channel $\alpha_2\delta_2$ -a and that hybridizes under conditions of high stringency to the sequence of nucleotides set forth in SEQ ID NO:1;
- (c) a nucleotide sequence varying from the nucleotide sequence specified in (a) or (b) as a result of degeneracy of the genetic code;
- (d) ~~a sequence of nucleotides having at least 95% sequence identity or is exactly complementary to the nucleotide sequence set forth in SEQ ID NO:1;~~
- (e) fragments of (a), (b), c), or (d) that encodes polypeptide capable of forming a functional voltage-gated calcium channel.

3. (Originally Presented) A substantially pure polypeptide comprising an amino acid sequence as set forth in any one of SEQ ID NOS: 2 or 4.

4. (Currently Amended) A substantially pure polypeptide comprising an amino acid sequence encoded by the ~~nucleotide sequence as set forth in one of as set forth in one of SEQ ID NOS:1 or 3.~~ nucleic acid molecule of claim 1.

5. (Originally Presented) A substantially pure polypeptide which has at least 80 % identity to the amino acid sequence of SEQ ID NO:2, which may include up to N_a amino acid alterations over the entire length of SEQ ID NO:2, wherein N_a is the maximum number of amino acid alterations, and is calculated by the formula

$$N_a = X_a - (X_a Y),$$

in which X_a is the total number of amino acids in SEQ ID NO:2, and Y has a value of 0.80, wherein any non-integer product of X_a and Y is rounded down to the nearest integer prior to subtracting such product from X_a .

7. (Originally Presented) An expression vector comprising the nucleic acid molecule of claim 1 operably linked to a regulatory nucleotide sequence that controls expression of the nucleic acid molecule in a suitable host cell.

8. (Originally Presented) A recombinant host cell transfected by the expression vector of claim 8.

9. (Currently Amended) A method for detecting the presence of a variant nucleic acid sequence of $\alpha 2\delta 2$ -a in a biological sample, comprising the steps of: (a) hybridizing to nucleic acid material in said biological sample the nucleic acid molecule of claim 1 under conditions favoring the formation of a hybridization complex; and (b) detecting said hybridization complex; wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

11. (Currently Amended) A method for detecting the $\alpha 2\delta 2$ -polypeptide of claim 4 [variant] in a first biological sample, comprising the steps of: (a) contacting a detectable probe with said biological sample suspected of containing said [variant] polypeptide under conditions favoring the formation of a complex between said probe and any said [variant] polypeptide; and (b) detecting said complex wherein the presence of said complex correlates with the presence of the desired ~~amino acid~~ polypeptide in said biological sample.

13. (Currently Amended) A method for treating or correcting a disease state caused by a dysfunctional human voltage-gated calcium channel mediated by the polypeptide of claim 3 ~~inhibiting human voltage-gated calcium channel $\alpha 2\delta 2$ -a subunit activity in a mammalian cell~~ comprising contacting the mammalian cell with an amount of a human voltage-gated calcium channel $\alpha 2\delta 2$ -a subunit inhibitor effective to inhibit calcium influx in the mammalian cell.

14. (Originally Presented) The method of claim 13, wherein the inhibitor is selected from the group consisting of an antibody which selectively binds the human voltage-gated calcium channel $\alpha 2\delta 2$ -a subunit polypeptide, an antisense nucleic acid which binds a

nucleic acid encoding human voltage-gated calcium channel $\alpha_2\delta_2$ -a subunit polypeptide and a dominant negative human voltage-gated calcium channel $\alpha_2\delta_2$ -a subunit polypeptide.

15. (Originally Presented) A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with increased or decreased voltage regulated calcium influx mediated by a human voltage-gated calcium channel comprising:

- (i) providing a cell expressing a human voltage-gated calcium channel $\alpha_2\delta_2$ -a subunit polypeptide;
- (ii) contacting the cell with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, to thereby cause a first amount of voltage regulated calcium influx into the cell; and
- (iii) determining a test amount of voltage regulated calcium influx as a measure of the effect of the lead compounds for a pharmacological agent on the voltage regulated calcium influx mediated by a human voltage-gated calcium channel, wherein (a) the test amount of voltage regulated calcium influx which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces voltage regulated calcium influx and (b) wherein a test amount of voltage regulated calcium influx which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases voltage regulated calcium influx.

16. (Originally Presented) The method of claim 15, further comprising loading said cell with a calcium-sensitive compound which is detectable in the presence of calcium, wherein the calcium-sensitive compound is detected as a measure of the voltage regulated calcium influx.

17. (Currently Amended) A method for identifying compounds which selectively bind [a] the polypeptide of claim 4 or a functionally effective isoform thereof ~~human voltage-gated calcium channel $\alpha_2\delta_2$ -subunit isoform~~ comprising, (i) providing a test cell preparation, wherein said cell expresses said polypeptide or said isoform thereof ~~a human voltage-gated calcium channel $\alpha_2\delta_2$ -subunit isoform~~, (ii) providing a control cell preparation, wherein said cell expresses a human voltage-gated calcium channel non- $\alpha_2\delta_2$

subunit isoform, with the proviso that the cell in the cell preparation is identical to the test cell except for the expression of a polypeptide other than the polypeptide expressed in said test cell preparation ~~non- $\alpha 2\delta 2$ isoform being expressed~~, (iii) contacting the test cell preparation and the control cell preparation with a compound, and (iv) determining the binding of the compound to the test cell preparation and the control cell preparation, wherein a compound which binds the test cell preparation but does not bind the control cell preparation is a compound which selectively binds the polypeptide of claim 4 or a functional equivalent isoform thereof ~~human voltage-gated calcium channel $\alpha 2\delta 2$ subunit isoform~~.

19. (Currently Amended) A diagnostic method for predicting an oncogenic potential of a sample of cells, comprising:

- (a) determining, in the sample, levels of expression of a gene product expressed from the nucleic acid molecule according to claim 1 a ~~nucleotide sequence of SEQ ID NO. 1 or 3 or a sequence which hybridizes to one of the above sequences or its complement~~, wherein excessive or insufficient levels of expression of said gene product relative to normal is predictive of the oncogenic potential of said cells.

20. (Originally Presented) An isolated nucleic acid molecule of an alternative splicing variant of a human voltage-gated calcium channel subunit, comprising a sequence of nucleotides encoding a voltage-gated calcium channel $\alpha 2\delta 2$ -b subunit selected from the group consisting of:

- (a) a sequence of nucleotides that encodes a human voltage-gated calcium channel $\alpha 2\delta 2$ -b subunit residues and comprises the sequence of nucleotides set forth in SEQ ID NO:3;
- (b) a sequence of nucleotides that encodes a human voltage-gated calcium channel $\alpha 2\delta 2$ -b and that hybridizes under conditions of high stringency to the sequence of nucleotides set forth in SEQ ID NO:3;
- (c) a nucleotide sequence varying from the nucleotide sequence specified in (a) or (b) as a result of degeneracy of the genetic code;
- (d) a sequence of nucleotides having at least 95% sequence identity or is exactly complementary to the nucleotide sequence set forth in SEQ ID NO:3;
- (e) fragments of (a), (b), c), or (d) that encodes polypeptide capable of forming a functional voltage-gated calcium channel.